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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/824,584	04/08/2004	Stephen Hart	20040117.ORI	6640

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EXAMINER	
EPPS FORD, JANET L	
ART UNIT	**PAPER NUMBER**
1633	

MAIL DATE	DELIVERY MODE
11/15/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/824,584	HART ET AL.	
	Examiner	Art Unit	
	Janet L. Epps-Ford	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6,9-11,17-26,31-33 and 39-41* is/are pending in the application.

4a) Of the above claim(s) *3,4 and 39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5,6,9-11,17-26,31-33,40 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-2, 5-6, 9-11, 17-26, 31-33 and 40-41 are presently under examination. Claims 3-4, and 39 are withdrawn from further consideration pursuant to 37 CFR 1.142(b).

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Specification

3. The objection to the specification set forth in the prior Office Action is withdrawn in response to Applicant's amendment to remove the embedded hyperlinks and/or other form of browser-executable code from page 22.

Oath/Declaration

4. The objection to the oath or declaration set forth in the prior Office Action is withdrawn in response to Applicant's submission of supplemental oath/declaration in compliance with CFR 1.67(a)(2).

Response to Arguments

Claim Rejections - 35 USC § 112

5. Claims 1-2, 5-6, 9-11, 17-26, 31-33 and 40-41 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for suppressing the expression of a selected gene in a cell *in vitro,* or for modulating the expression of a selected gene in a cell *in vitro*, comprising introducing into the cell a molecule comprising a nucleic acid binding portion and a polypeptide or peptidomimetic repressor portion, wherein said repressor is all or a portion of a component of a histone

acetyltransferase, does not reasonably provide enablement for practicing the claimed methods *in vivo* in a human subject with the production of a therapeutic effect as a result of practicing the claimed methods. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

6. Applicant's arguments filed 9-11-2007 have been fully considered but they are not persuasive. Applicants traversed the instant rejection on the grounds that applicants believe a skilled person would have been well aware of approaches suitable for delivering the claimed molecules before the present application in view of the numerous publications in that field available prior to the 12 October 2001 priority date of the present application. Moreover, Applicants specifically note the example of the Genasense antisense phosphorothioate oligonucleotide compound directed towards the human bcl-2 mRNA sequence, and termed Oblimersen (Herbst et al., 2004).

7. Contrary to Applicant's assertions, the scope of the instant clams comprises administering a molecule comprising a nucleic acid binding portion comprising an oligonucleotide or oligonucleotide mimic or analogue and a peptide or peptidomimetic. The reference provided by Applicants describes a phosphorothioate antisense oligonucleotide, however the instant claims are drawn to a method comprising the introduction of an oligonucleotide or oligonucleotide mimic or analogue and a peptide or peptidomimetic. Applicants have not provided any evidence that the same method of *in vivo* delivery of the antisense compounds of Herbst et al. (2004) could be applied directly to the full scope of molecules encompassed by the instant claims, wherein the

molecules of the instant invention are structurally distinct from the phosphorothioate oligonucleotides of Herbst et al.

Contrary to Applicant's assertions, although there are many references teaching the *in vivo* delivery of antisense oligonucleotides, however, the scope of the instants read on the *in vivo* delivery of oligonucleotides, analogues, or mimic linked with peptides or peptidomimetic molecules. Moreover, the breadth of the claimed invention encompasses methods of medical treatment, including the treatment of cancers in which oncogenes play a role (see the bridging paragraph of pages 32-33). According to Applicant's specification, see page 32, beginning at line 14, the method of the claimed invention can be used to suppress or inactivate the expression of a gene whose expression it is desirable to suppress or inactivate. Such genes include oncogenes, viral genes including genes present in proviral genomes and so the method in relation to animals may constitute a method of medical treatment.

The specification as filed provides only prophetic guidance for using the claimed oligo/peptide (or analogues or mimics thereof) in an *in vivo* method of treating a patient.

As stated in the prior Office Action, the therapeutic use of oligonucleotides *in vivo,* the state of the art, even after the effective filing date of the instant application (10/11/2001), indicates that delivery of these oligonucleotide compositions for therapeutic purposes "remains an important and inordinately difficult challenge (Chirila et al., 2002; see abstract)." Chirila et al. page 327, last paragraph) teach that "[T]he in vivo delivery techniques chiefly used at the present, i.e. infusion or injection of naked molecules and liposomal systems, do not assure adequately long-term maintenance of

ODNs (oligonucleotides) in tissues," which is required to achieve therapeutic effects. As a conclusion to the review of Chirila et al., the state of oligonucleotide based drug therapy is summarized by the statement: "the antisense strategy only awaits a suitable delivery system in order to live up to its promise." Therefore, the efficacy of antisense based therapies hinges upon the ability to deliver a sufficient amount of oligonucleotide, to the appropriate tissues, and for a sufficient period of time, to produce the desired therapeutic effect. So far, it appears that all of the developments in antisense based therapies have not been sufficient to overcome this one basic obstacle, drug delivery. Furthermore, Applicant's specification does not provide actual working examples or guidance so that the skilled artisan can deliver the pharmaceutical compositions of the claimed invention to target tissues successfully, to produce the desired therapeutic result without undue experimentation.

8. Claims 1-2, 5-6, 9-11, 17-26, 31-33 and 40-41 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (Written Description).

9. Applicant's arguments filed 9-11-2007 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that Applicant's examples make it clear that the inventors developed methods for modulating or suppressing gene expression as claimed in claims 1 and 2 by introducing a molecule

comprising nucleic acid binding portion of an oligonucleotide or oligonucleotide mimic and an expression modulating portion comprising a polypeptide or peptidomimetic.

Moreover, Applicants argue that in view of the 2006 decision in *Falkner v Inglis (448 F.3d 1357 C.A. Fed. 2006)* that "a claim would not be invalidated on Section 112 written description grounds simply because the application did not contain examples covering the full scope of the claim language.." Furthermore, Applicants argue that "actual reduction to practice is not required." (see page 16) Contrary to Applicant's assertions, the *Falkner v Inglis (2006)* decision also states that: "[t]he 'written description' requirement states that the patentee must describe the invention; it does not state that every invention must be described in the same way. As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution." Id. at 1358. Indeed, the forced recitation of known sequences in patent disclosures would only add unnecessary bulk to the specification. Accordingly we hold that where, as in this case, accessible literature sources clearly provided, as of the relevant date, genes and their nucleotide sequences (here "essential genes"), satisfaction of the written description requirement does not require either the recitation or incorporation by reference." The examiner agrees that Applicants are not responsible for setting forth what is commonly known in the prior art. However, in the instant case, it is unclear what prior art structures Applicants are relying upon to support their assertion that the full scope of the claimed invention is adequately described as in the case of *Falkner v. Inglis.* In the instant case, the claims are drawn to a broad genus of molecules comprising a variety of activities, however there is not

clear structural correlation between the amino acid structures and/or nucleic acid sequence structures of the full scope of molecules of the instant invention, and the corresponding activities. In the instant case, the claims are drawn to a complex comprising an oligonucleotide or mimic (covalently?) and a peptide or peptidomimetic wherein the complex suppresses activity of a selected gene. Contrary to Applicant's assertions, the examiner is unaware of accessible literature sources that would suggest of clearly define the complexes of the claimed invention. Applicants are invited to assist the examiner in defining the literature disclosing the structures of the complexes useful in the claimed invention. As a specific example, the examiner is unaware of the full scope of ***portions*** of a polypeptide that binds to or facilitates the recruitment of a histone acetyltransferase complex, as recited in instant claim 5, which depends from claim 1 or 2. What portions of these polypeptides are useful in the claimed invention? Are there conserved amino-acid structures? There is no reference to the prior art that would assists the examiner in understanding the scope of the claimed invention.

See MPEP § 2163, which states "[A] biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence."

Due to the significant breadth of the instant claims, and the limited guidance provided in the specification as filed *and in the prior art*, in regards to describing the structures of the full scope of compounds encompassed by the instant claims, the

skilled artisan would have to resort to further experimentation in order to identify the full scope of compounds encompassed by the instant claims.

Conclusion

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps-Ford whose telephone number is 571-272-0757. The examiner can normally be reached on M-F, 10:00 AM through 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Janet L. Epps-Ford/
Primary Examiner
Art Unit 1633

JLE